



# FDA Drug Approval: A Black and White Issue?

## Citation

FDA Drug Approval: A Black and White Issue? (2006 Third Year Paper)

## Permanent link

<http://nrs.harvard.edu/urn-3:HUL.InstRepos:8852196>

## Terms of Use

This article was downloaded from Harvard University's DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at <http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA>

## Share Your Story

The Harvard community has made this article openly available.  
Please share how this access benefits you. [Submit a story](#).

[Accessibility](#)

Microsoft Word 10.0.6612;

FDA Drug Approval: A Black and White Issue?

Stephanie A. Yonker

Class of 2006

April 2006

Submitted in Satisfaction of the Course Requirement

## ***Abstract***

The FDA should judiciously limit the FDA approval of race-specific drugs to situations in which the utilization of racial categories is based on statistically significant scientific data and necessity and, in such cases, the meaning of race utilized should be defined. The term “race” is an inherently ambiguous social construct making the FDA approval of race-specific drugs and use of race in FDA approval decisions dangerous with debatable scientific legitimacy. Further, race is generally used in drug trials as a crude proxy for the determination of genetic variation, which tends to be both over and under-inclusive in determining the efficacy or safety of a drug for any individual. The limited genetic validity of race is confounded by the reality that many population differences between races may be the result of socio-economic and environmental factors that are not *per se* innate or inherent to any racial population. While the scientific validity of race as biologically significant classification is debatable, the general public is likely to interpret the governmental approval of the drug by the FDA as evidence of inherent genetic differences between racial groups that will serve to only further racial discrimination and eugenic ideologies. Thus, the FDA should proceed cautiously by narrowly tailoring the use of race in the FDA approval of new drugs and require a showing of statistically significant scientific data and the need to rely on race because of the lack of genetic markers.

## ***Introduction***

Life-Saver<sup>1</sup>

### INDICATIONS AND USES

Life-Saver is indicated for treatment in *self-identified Black patients* to improve survival, prolong time to hospitalization, and to improve patient-reported functional status.<sup>2</sup>

---

<sup>1</sup>Life-Saver is merely a hypothetical drug used for discussion in this paper.

<sup>2</sup>The indication and use statement for Life-Saver is based on the indication and use statement for the first “ethnic” drug BiDil® provided as a part of the patient information sheet mandated by 21 U.S.C. § 352 (2004). The indication and use statement for BiDil® reads, “BiDil is indicated for treatment of heart failure as an adjunct to standard therapy in self-identified Black patients to improve survival, prolong time to hospitalization for heart failure, and to improve patient-reported

Explicitly with our hypothetical drug Life-Saver's indication and use guidelines, the use of the drug is approved for treatment in self-identified Blacks. While the drug purports to improve survival and the general health of patients, this potentially life saving drug is available under Food and Drug Administration ("FDA") approval solely to self-identified Blacks. While it is true that FDA guidelines allow prescribing drugs off-label, which would allow doctors to distribute the drug to individuals who do not self-identify as Black, many doctors may be hesitant to prescribe to a non-Black person. Doctors may regard the drug as a Black-only treatment without further investigation into drug research data on a racially diverse patient clinical trial, clinical trials targeted towards the racial group identified by their patient, or extensive scientific knowledge regarding the mechanism of drug function. As a result, patients who identify with White, Hispanic, Asian, and other racial groups would be denied or severely limited in their access to our hypothetical drug, Life-Saver, even though they may benefit from the use of the drug with increased survival and improved general health. Our hypothetical Life-Saver may seem like only an academic, intellectual exercise into the use of race in scientific research and the ramifications on society. However, with the FDA approval of the heart medication BiDil®, with a use and indication statement very similar to our hypothetical drug, Life-Saver, the debate has moved beyond the realm of an abstract academic debate to the real world.<sup>3</sup>

Currently, peer reviewed scientific journals report that over twenty-nine different medicines (or combination of medicines) possess differences in safety and efficacy based on race or ethnicity.<sup>4</sup> Although these differences based on race and ethnicity are still controversial and strenuously debated within the scientific community, the movement to discover and market race and ethnic specific drugs is growing. The discovery and FDA approval of drugs, such as BiDil®, which appears to have a racially differential effect on self-identified Blacks,

---

functional status." BiDil® Product Insert (2005), *available at* <http://www.bidil.com/pdf/PI.pdf>.

<sup>3</sup>FDA, FDA APPROVES BiDIL HEART FAILURE DRUG FOR BLACK PATIENTS (June 23, 2005), *available at* <http://www.fda.gov/bbs/topics/NEWS/2005/NEW01190.html>.

<sup>4</sup>Sarah K. Tate & David B. Goldstein, *Will tomorrow's medicines work for everyone?*, 36 NAT. GENETICS S34, S34 (2004).

shines as a beacon of hope to address potential racial differences in medical response to drugs and narrowing the unequal access to medical services. The development of race specific drugs highlights potentially distinct medical needs in a racial community. The development of drugs such as BiDil® and the development of FDA guidelines permitting approval of such race-specific drugs, however, should also raise serious concerns as to the appropriateness of using race in drug development and the economic motives driving drug companies, at least in part, to target racial groups.

Targeting a drug to a particular racial group creates financial incentives for pharmaceutical companies that may impede access to safe, effective, and cheap treatment to everyone who could benefit regardless of race. While narrowing the field of potential drug users to a minority racial group may seem to narrow the potential revenue generation abilities of a drug, there may be financial incentives lurking in the background motivating the development of racial drugs. For example, in the case of BiDil®, intellectual property rights may have in part driven the manufacturer to test the drug in self-identified Blacks.<sup>5</sup> In the initial clinical study of BiDil®, the drug appeared to have an impact on mortality in a mixed-racial population, however, “the differences was only of border-line statistically significance.”<sup>6</sup> In the second clinical trial, the FDA voted against approving the drug in a mixed-racial population in a vote of nine to three because “there were too many variables specified in the protocols at primary end points for them to interpret the . . . data with any degree of certainty.”<sup>7</sup> After the advisory committee denied approval, the BiDil® inventor went back and reanalyzed the clinical data from both clinical trials, including 395 black patients and 1024 white patients, and found that the active ingredients of BiDil® were “particularly effective” in black patients.<sup>8</sup> The U.S.

---

<sup>5</sup> See Jonathan Kahn, *How a Drug Becomes “Ethnic”: Law, Commerce, and the Production of Racial Categories in Medicine*, 4 YALE J. HEALTH POL’Y, L. & ETHICS 1 (2004).

<sup>6</sup> *Id.* at 12.

<sup>7</sup> *Id.* at 15.

<sup>8</sup> *Id.* at 17. See Carson P. et al, *Racial differences in response to therapy for heart failure: analysis of the vasodilator-heart failure trials*, 5 J. OF CARDIAC FAILURE 178 (1999).

Patent and Trademark Office issued a new patent for the use of BiDil® in African-Americans finding that the “race-specific method of treatment to be a ‘non-obvious’ extension” of the earlier patent application for the drug.<sup>9</sup> Reframing BiDil® in terms of race, granted BiDil® creators an opportunity to amend their FDA new drug application and extend intellectual property rights. As a result of the race-specific method of treatment, BiDil® manufacturers will have patent protection until 2020, rather than 2007.<sup>10</sup> Targeting BiDil® to self-identified Blacks granted BiDil® manufacturers thirteen more years of patent protection, while a treatment regime for all patients could not have extended the company’s intellectual property rights.<sup>11</sup> Further, while the indication and use statement indicates the drug is FDA approved as a treatment for self-identified Blacks, doctors may still prescribe the drug off-label to other racial groups, recouping at least some of the costs of targeting the drug for FDA approval to a smaller population of patients.<sup>12</sup> The market of a drug and attempt to achieve FDA approval of a race-specific drug may become a business strategy of pharmaceutical companies motivated by financial incentives, rather than purely scientific data. As more drugs are reported to possess differences in safety and efficacy based on race, the economic costs to U.S. patients and health care insurers in terms of paying higher prices for patented drugs will only grow.

In regards to the appropriateness of race generally in drug discovery, the limited FDA approval of potential life saving drugs for use in particular racial and/or ethnic groups raises serious questions of fairness and equality of health care and drug access that cuts both ways in favor and against race-based therapeutics.<sup>13</sup>

---

<sup>9</sup>Kahn, *supra* note 5, at 32.

<sup>10</sup>Jonathan Kahn, *Misreading Race and Genomics after BiDil*, 37 NAT. GENETICS 655, 655 (2005). While beyond the scope of this paper, the policy of the U.S. Patent and Trademark Office regarding the use of race in patent prosecution should be reevaluated and revised to limit the use of race-specific claims.. One could argue that a claim to a racial subpopulation is obvious and thus unpatentable when compared to prior art disclosing data demonstrating general drug effectiveness regardless of race; however, as evidenced by BiDil, the PTO currently regards a claim to a racial subpopulation non-obvious even with prior art demonstrating efficacy in humans generally.

<sup>11</sup>M. Gregg Bloche, *Race-Based Therapeutics*, 351 NEW ENG. J. OF MED. 2035, 2036 (2004).

<sup>12</sup>See Michael I. Krauss, *Loosening the FDA’s Drug Certification Monopoly: Implications for Tort Law and Consumer Welfare*, 4 GEORGE MASON L. REV. 457, 470 (1996). For example in the case of BiDil, some researchers have indicated that they are “absolutely confident that BiDil will work for patients other than African Americans” and should be given to patients regardless of race with nitric oxide deficiencies. David Rotman, *Race and Medicine: Population Genomics is Expanding our Knowledge of Human Diversity. What Role Should Race Have in Drug Development*, Technology Review (April 2005), available at <http://www.technologyreview.com/read.article.aspx?id=14301&ch=biotech>

<sup>13</sup>See Erik Lillquist and Charles A. Sullivan, *The Law and Genetics of Racial Profiling in Medicine*, 39 Harv. C.R.-C.L. L.

Notably, minority populations traditionally have less access to health care services, and most FDA-approved drugs currently on the market were tested in clinical trials on a patient populations consisting primarily of Caucasians.<sup>14</sup> There are still substantial inequalities and unfairness in access to health care as a result of socioeconomic status and discrimination that disproportionately affect individuals based on race. Thus, drugs targeted to traditionally underserved minority racial groups could improve general health care services for these populations by increasing funding to explore diseases that disproportionately affect the minority individuals and increase the knowledge in the minority community of treatment options. However, a fundamental question remains whether the recent embrace of race-based therapeutics by the medical community and FDA is justified scientifically, and whether self-identified race and/or ethnicity, alone as a proxy for genetic variation, should be utilized as categories to distinguish individuals in medical research and FDA drug approval processes. Further, beyond the scientific legitimacy of use of race as a proxy for genetic variation, the use of race as a basis of FDA approval creates its own fairness and equality issues by potentially limiting access of other racial groups to drugs and by reinforcing and legitimatizing dangerous social beliefs that race represents inherent, genetic differences, which could serve as a basis for further racial discrimination. There may be circumstances where a drug, which fails to meet FDA effectiveness and safety guidelines for the general population, but does for a discrete racial population, should be approved by the FDA with labeling indicating racial differences in efficacy or side-effects upon a showing of statistically significant clinical data denoting differences between racial populations. However, the FDA should be cautious and should significantly limit the race-specific FDA drug approval applications to situations where there is a scientific basis and necessity for the use of race because no other population markers are available (i.e. genetic markers), and in such cases, the meaning of race utilized should be clearly defined.

The judicious and limited FDA approval of race-specific is appropriate based on four lines of reasoning that

---

Rev. 391, 396-97 (2004); *see also* Troy Duster, *Race and Reification in Science*, 307 Sci. 1050, 1050 (2005).

<sup>14</sup>See David Wendler et al., *Are Racial and Ethnic Minorities Less Willing to Participate in Health Research?*, PLOS MED. 3(2): 1, 7-8 (2006).

will be discussed in this paper. First, race, particularly self-identified race, is an inherently ambiguous social construction making use in FDA approval reviews dangerous. Secondly, race is merely a crude proxy for the determination of genetic traits, which results in over and under-inclusion of certain individuals in categories where a drug may be efficacious. Third, population differences based on race may often be the partial result of socio-economic and environment factors, not genetic factors, weakening the scientific argument that race alone is an appropriate indicator of drug efficacy or risk. Fourth, while arguably the scientific community may be able to practice restraint and recognize the limitations of using race, the lay community may interpret differences in disease risk and FDA approval of race specific drugs as inherent differences at the genetic level among racial groups and serve as the basis for discriminatory and eugenic policies. Because of the foregoing reasons, as will be discussed in the final section of this paper, the FDA should revise its policies regarding the FDA drug approval race-specific drug applications to situations where race is clearly defined and there is clear scientific basis and necessity to ensure that potentially life saving drugs are made available to all regardless of race.

## **Race: An Ambiguous Social Construct**

Undeniably, race is an important and volatile social construct within the United States. Race continues to serve as the basis for discrimination and represents a key dimension of the economic and social stratification of our society. Race not only plays an important role within American society generally, but also within the medical and health care communities. For example, Blacks in the United States generally receive lower quality health care than White patients. A study in the *New England Journal of Medicine* monitoring Medicare



beneficiaries reported that Black patients were less likely to receive health care services from a board certified physician than White patient.<sup>15</sup> Further, the rates of early screening for most diseases was lower in Black patients compared to White patient, while Black patients were more likely to be diagnosed with a disease at relatively advanced stages.<sup>16</sup> Another study reported in the *New England Journal of Medicine* indicated that Black patients were significantly less likely to undergo angioplasty and bypass surgery than White patients—a difference in application of coronary-revascularization procedures that could not be explained by clinical characteristics of the disease.<sup>17</sup> Race in the United States as evidenced by these studies is a social construct with real, significant implications in one’s access to quality health care.

While Americans recognize the power of the race construct in society, there is substantial ambiguity in defining race and which characteristics and factors should be considered in the definition of race. Further, the guidelines delineating the contours of the race are not static, but have changed throughout United States history. Currently the FDA recommends the use of the standardized Office of Management and Budget (OMB) race and ethnicity categories for data collection (Policy Directive 15).<sup>18</sup> The OMB procedures recommend using a two-question format for gathering information on race and ethnicity. The first question to ask is whether the individual self-identifies with the Hispanic or Latino ethnic group.<sup>19</sup> The second question is whether the individual self-reports to be a member of one of five racial categories: (1) American Indian or Alaska Native, (2) Asian, (3) Black or African American, (4) Native Hawaiian or Other Pacific Islander, and (5) White.<sup>20</sup> The five different racial groups encompass individuals within each single racial group from diverse geographical ancestry. White reflects individuals with ancestry in Europe, Middle East,

---

<sup>15</sup> See Peter B. Bach et al., *Primary Care Physicians Who Treat Whites and Blacks*, 351 NEW ENG. J. OF MED. 575 (2004) (all patient were Medicare beneficiaries).

<sup>16</sup> *Id.* at 583.

<sup>17</sup> See Eric D. Peterson et al., *Racial Variation in the Use of Coronary-Revascularization Procedures — Are the Differences Real? Do They Matter?*, 336 NEW ENG. J. OF MED. 480 (1997) (all patients utilized the Duke University Medical Center).

<sup>18</sup> See FDA, GUIDANCE FOR INDUSTRY: COLLECTION OF RACE AND ETHNICITY DATA IN CLINICAL TRIALS (Sept. 26, 2005), available at [www.fda.gov/CbER/gdlns/racethclin.htm](http://www.fda.gov/CbER/gdlns/racethclin.htm).

<sup>19</sup> See *id.* at 5.

<sup>20</sup> See *id.*

or North Africa, while Asian includes people from geographical areas ranging from India and Pakistan to Japan.<sup>21</sup> Beyond the five racial categories, the OMB allows an individual to identify themselves with more than one racial group.

The current guidelines dividing U.S. citizens into five racial groups and one ethnic group was established in 1997 by the OMB Federal Standards for Racial and Ethnic Data in preparation for the 2000 Census. This 1997 Policy Directive 15 modified a 1977 Directive in which Asian and Pacific Islander was considered a single racial group to recognize Asian as a separate racial group from Native Hawaiian and Other Pacific Islander.<sup>22</sup> Further, the 1997 Policy Directive 15 allowed multiracial individuals to mark on or more racial categories on forms for the first time.<sup>23</sup> Before this change, individuals of mixed racial ancestry were forced to select only race, even if they self-identified with multiple racial groups. The change in U.S. policy regarding classification of race is not the first. The federal government utilized race characterization in census calculations since 1790.<sup>24</sup> The Census Bureau has utilized multiple methods through history to categorize race based on national origin, tribal associations, and physiological characteristics such as skull size, skin color, and facial features.<sup>25</sup> Historically, terms like mulatto, quadroon, octoroon were utilized to classify individuals based on percentage of Black ancestry, which emerged as an extension of the “one drop” of African ancestry determining racial category.<sup>26</sup> Further, in the beginning of the twentieth century, Jews were classified as a distinct, non-White race.<sup>27</sup> As the U.S. Census guidelines regarding categorization of race illustrate, race is an ambiguous concept subject to societal change over time.

The struggle and changing social norms regarding defining race in American culture is further illustrated

---

<sup>21</sup> See OFFICE OF MGMT. & BUDGET, OMB STANDARDS FOR MAINTAINING, COLLECTING, AND PRESENTING FEDERAL DATA ON RACE AND ETHNICITY (Oct. 30, 1997), available at [www.Whitehouse.gov/omb/inforeg/re\\_app-a-update.pdf](http://www.Whitehouse.gov/omb/inforeg/re_app-a-update.pdf)

<sup>22</sup> Vickie M. Mays et al., *Classification of Race and Ethnicity: Implications for Public Health*, 24 ANNUAL REV. OF PUBLIC HEALTH 83 (2003).

<sup>23</sup> *Id.*

<sup>24</sup> *Id.* at 88.

<sup>25</sup> Sandra Soo-Jin Lee et al., *The Meaning of “Race” in the New Genomics: Implications for Health Disparities Research*, 1 YALE J. HEALTH POL’Y, L. & ETHICS 33, 37 (2001).

<sup>26</sup> Mays, *supra* note 22, at 88.

<sup>27</sup> *Id.*

within Supreme Court jurisprudence. In *Saint Francis College v. Al-Khazraji*, 481 U.S. 604 (1987), the Supreme Court of the United States wrestled with the problem of defining the term “race.” Al-Khazraji was a person of Arab ancestry who alleged being terminated from his position as a university professor based on race discrimination and brought a cause of action under 42 U.S.C. § 1981.<sup>28</sup> § 1981 grants all person the same rights to make and enforce contracts as White citizens.<sup>29</sup> Although § 1981 does not use the word race in its text, the Court has construed the section to forbid all racial discrimination when making private and public contracts.”<sup>30</sup> Saint Francis College argued that Al-Khazraji falls within the classification boundaries of a Caucasian individual and, therefore, according to St. Francis, Al-Khazraji could not allege racial discrimination when the college denied tenure in favor of another Caucasian professor.<sup>31</sup> The Court states that race should be determined as would be understood by one when § 1981 became law in the nineteenth century. The Court continues by noting that encyclopedias and dictionaries in the nineteenth century considered Mongolians, Russians, Spanish, Italians, Germans, Norwegians, Swedes, Gypsies, Anglo-Saxon, and Arabs as separate races.<sup>32</sup> Recognizing that the meaning of the term race has changed over time, the Supreme Court interprets the legislative intent of the § 1981 statute to protect individuals from intention discrimination based on their ancestry or ethnic characteristics and hold that a person of Arab ancestry is protected from discrimination under §1981.<sup>33</sup>

The *Al-Khazraji* case illustrates two important points. First, the reality that race is a social construct that is subject to changing meaning over time as cultural attitudes change. Within the past hundred years, the notion of race and the term “Caucasian” has changed drastically. Individual countries in Europe were

---

<sup>28</sup>See *St. Francis College v. Al-Khazraji*, 481 U.S. 604, 604 (1987).

<sup>29</sup>See *id.* at 609.

<sup>30</sup>See *Runyon v. McCrary*, 427 U.S. 160, 168 (1976).

<sup>31</sup>See *Al-Khazraji*, 481 U.S. at 609-10.

<sup>32</sup>See *id.* at 611-12.

<sup>33</sup>See *id.* at 613.

considered populated by distinct races, rather than the assumption today that Europeans are members of a single race. The second point is the breadth and ambiguity of terms such as Caucasian. Caucasian, according to the 1997 Policy Directive 15, includes any individual with ancestry from Europe, Middle East, or North Africa. As evidenced by the *Al-Khazraji* case, the term race is ambiguous. § 1983 used the term “White citizen” in attempt to set a threshold for right to contract. However, through the expansive scope and ambiguity associated with current racial categories, the text of the statute is unable to articulate its intended purpose. Whether one wants to label the discrimination as ethnic or race (noting that Arab, for example, is not recognized as an ethnic group in the 1997 Policy Directive 15), American society view some subset of our current social construct of race, Caucasian, differently.<sup>34</sup> Race is an inherently ambiguous social construct as evidenced by the contours of the term and classification of race in the United States throughout its history.

The assignment of an individual to a racial group is not necessarily a “Black and White” issue. The use of self-identification in determining race assumes that individuals know their complete racial ancestry. First, self-identification by an individual with a racial or ethnic group may not represent the true complexity of a person’s ancestry. Some studies indicate that African Americans possess “a range of European ancestry that extends from nearly 0 percent to greater than 50 percent”<sup>35</sup>, with an average according to other studies of 20 percent.<sup>36</sup> Additionally, Latinos often comprise an ancestry from three different continents, Europe, Africa, and America, in variable proportions.<sup>37</sup> Secondly, many Americans identify with multiple racial categories of ancestry. According to the 2000 Census, over 6.8 million Americans self-identified with two or more races.<sup>38</sup> There are no data regarding the growth of the multiracial population in the United States (the 2000

---

<sup>34</sup>The OMB specifically declined to add Arab or Middle Eastern as an ethnic group in the 1997. OFFICE OF MGMT. & BUDGET, REVISIONS TO THE STANDARD FOR THE CLASSIFICATION ON FEDERAL DATA ON RACE AND ETHNICITY, (Oct. 30, 2000), available at <http://www.census.gov/population/www/socdemo/race/Ombdir15.html>.

<sup>35</sup>Moumita Sinha et al., *Self-reported Race and Genetic Admixture*, 354 NEW ENG. J. OF MED. 421 (2006).

<sup>36</sup>Xiaofeng Zhu et al., *Admixture mapping for hypertension loci with genome-scan markers*, 37 NAT. GENETICS 178 (2005).

<sup>37</sup>Esteban Gonzalez Burchard et al., *Latino populations: a unique opportunity for the study of race genetics, and social environment in epidemiological research*, 95 AM. J. OF PUB. HEALTH 2161 (2005).

<sup>38</sup>See Nicholas A. Jones and Amy Symens Smith, *The Two or More Races Population: 2000*, Census 2000 Brief, November

Census was the first where an individual could indicate membership in more than one race). However, based on Census Bureau research regarding children living in mixed-racial families, the population of multiracial individuals is likely growing. In 1970, only 460,000 children lived in mixed-race families, while in 1990 that number increased to 1,927,496 children.<sup>39</sup> The concept of distinct racial categories is confounded by the increasing number of multiracial individuals and the number of individuals that with ancestry from multiple racial groups even though they self-identify with one racial group. With the ever changing definition of race and the further growth of a multiracial population within the U.S., “it is extraordinarily difficult to classify individuals accurately and consistently for the purposes of identifying differences in drug effects” during clinical trials.<sup>40</sup> Recognizing race as an evolving social construct, the FDA and the health care profession should be hesitant and cautious about relying on race during clinical trials and in the FDA drug approval process.

## Race and Genetics

Almost since the dawn of modern evolutionary theory and genetics, people have attempted to validate social and cultural racial distinction by showing that the categorization of individuals was also based on biologi-

---

2001 page 2.

<sup>39</sup>See U.S. CENSUS BUREAU, QUESTIONS AND ANSWERS FOR CENSUS 2000 DATA ON RACE (Mar. 14, 2001), *available at* <http://www.census.gov/Press-Release/www/2001/raceqandas.html>. “The number of children in mixed-race households was obtained by cross-tabulating the race of the child by the race of the mother and father in married-couple households for the four major race groups (White; Black; American Indian, Eskimo and Aleut; and Asian and Pacific Islander). Children under 18 years old in married-couple families were identified as residing in a mixed-race household if the race for the parents, step-parent or unmarried partner and child living in the household are different, or if the race reported on the census form for the child differ from that of at least one parent, step-parent or unmarried partner.” U.S. CENSUS BUREAU, INTERRACIAL TABLES (Aug. 1, 2002), *available at* <http://www.census.gov/population/www/socdemo/interrace.html>. Please note, however, the number of multiracial families is likely not completely correlative with number of families with multiracial children as individuals who adopt bi-racially will also be included in this number, even though the adopted children may identify with a single racial group.

<sup>40</sup>Susanne B. Haga and J. Craig Venter, *FDA Races in Wrong Direction*, 301 SCI. 466, 466 (2003).

cally differences at the genetic level. Race has been used to justify the inferiority of groups of individuals based, not only on skin color and physiognomy, but also other characteristics, such as intelligence.<sup>41</sup> While race is an undeniably influential social construct, the scientific, biological basis of race and whether such a basis exists is much more contentious. On one hand, some scientists, as illustrated in an editorial in the *New England Journal of Medicine*, find that “race is a social construct, not a scientific classification[,]” arguing that “race is biologically meaningless.”<sup>42</sup> Conversely, other scientists, as illustrated in a companion editorial in the same issue of the *New England Journal of Medicine*, indicated that there are racial and ethnic differences in drug responses and diseases, which in part represent biological and in particular genetic differences.<sup>43</sup> Although the FDA has approved a drug for indications and uses in distinct racial groups, the scientific community is still actively debating the biological importance of race and the extent to which race should be used in scientific research to represent biological differences.

The premise that race is biologically meaningless or at the most of marginal significance is based upon the rational that an individual’s racial group membership does not necessarily correlate with an individual’s genotype. The recent sequencing of the human genome and some population genetics research support this proposition. According to the American Anthropological Association, modern humans “appear to be a fairly recent and homogeneous species” with “a high degree of similarities from a biological perspective.”<sup>44</sup> The homogeneous nature of the human species is evident from the reports by the Human Genome Project. Upon the mapping and sequencing of the human genome, researchers associated with the Human Genome Project highlighted the finding that the human population shares 99.9% of its DNA.<sup>45</sup> Of the 0.1% of DNA not

---

<sup>41</sup>Lillquist, *supra* note 13, at 409.

<sup>42</sup>Roberts S. Schwartz, *Racial Profiling in Medical Research*, 344 NEW ENG. J. OF MED. 1392, 1392 (2001).

<sup>43</sup>Alastair J.J. Wood, *Racial Differences in the Response to Drugs—Pointers to Genetic Differences*, 344 NEW ENG. J. OF MED. 1393, 1394 (2001).

<sup>44</sup>American Anthropological Association, *American Anthropological Association Response to OMB Directive 15: Race and Ethnic Standards for Federal Statistics and Administrative Reporting* (Sept. 1997), available at <http://www.aaanet.org/gvt/ombdraft.htm>.

<sup>45</sup>J. Craig Venter et al., *The Sequence of the Human Genome*, 291 SCI. 1304, 1348 (2001).

shared, greater genetic variation exists within racial and ethnic groups than between them.<sup>46</sup> To illustrate this finding, take for example a study comparing genetic variation among individuals with ancestry from the continents of Africa, Europe, and Asia. Approximately 85-90% of genetic variation is found within continental groups while only an additional 10-15% variation is found between them.<sup>47</sup> The extensive genetic variation among individuals within a continental group makes race an inappropriate proxy genetic risk during FDA clinical trials and drug approval process. For many genes, allelic variation within a racial population will often make race an inaccurate predictor of response to drugs or other medical treatments. Therefore, because of the high degree of overall sequence similarity among the human population and the substantial genetic variation within racial groups, some researchers argue that race is biologically meaningless or of marginal significance as applied to medical research.

While there is scientific data that race is of marginal biological significance, there is also data that clearly indicates that genetic traits and susceptibility to disease can differential effect racial populations. Scientific research supports the notion that race and ethnic categories do correlate or represent at least crude proxies for genetic traits that are distinguishable among racial populations. In some instances, the race of an individual will correlate with genetic characteristics that can result in differing propensities to develop a disease or response to a drug treatment regime. The scientific literature is full of report of race or ethnic differences in response to drugs and course of disease progression. For example, while the claims are controversial and there is no medical consensus, at least twenty-nine medicaments are claimed in peer reviewed scientific journals to have differences in safety and efficacy based on race or ethnicity.<sup>48</sup> Additionally, “[t]he human population is no homogeneous in terms of risk of disease.”<sup>49</sup> Scientists have identified the genetic basis of some disease that disproportionately affect special racial groups. Hemochromatosis, a disease that

---

<sup>46</sup>Haga, *supra* note 40, at 466.

<sup>47</sup>Lynn B. Jorde & Stephen P. Wooding, *Genetic variation, classification and ‘race’*, 36 NAT. GENETICS 528, 528 (2004).

<sup>48</sup>Tate, *supra* note 4.

<sup>49</sup>Neil Risch et al., *Categorization of humans in biomedical research: genes, race and disease*, GENOME BIOLOGY 3(7): comment2007.1, comment2007.1 (2002).

causes the body to absorb and store too much iron, “is associated with a mutant allele (C282Y) found in all European groups . . . , but is virtually absent in non-White groups.”<sup>50</sup> Cystic Fibrosis (CF), a disease causing several lung and nutritional deficiencies, is the result of another mutant allele ( $\Delta$ 508-CFTR), which primarily affects people Caucasian, with one out of every 3,200 White babies being affected. In comparison, within other racial groups, one in every 10,500 Native Americans, one in every 14,000 to 17,000 African Americans, and one in every 25,500 Asians are affected with CF.<sup>51</sup> Another example, Sickle Cell Anemia, is caused by a variant in the  $\beta$ -globin gene (*Hb S* variant), which results in abnormal red blood cell shape that can deprive tissue of oxygen and disproportionately affects Blacks in the United States. The disease affects approximately 72,000 individuals within the United States with one out of every 500 African Americans being affected by the disease.<sup>52</sup> Research has proven that some genetic diseases are more prevalent within distinct racial groups.

Race can also indicate differences in drug metabolism that will affect the efficacy of drug treatment regimes. Increasingly, researchers are identifying genes, whose allelic frequencies vary significantly between ethnic and racial populations, which influence the response and metabolism of drugs. For example, N-acetyltransferase 2 (“NAT2”) is an enzyme “involved in the detoxification of many carcinogens and the metabolism of many common drugs.”<sup>53</sup> Depending on an individual’s NAT2 genotype, they may be either a slow acetylator or rapid acetylator, which influences the rate of detoxification and drug metabolism. A recent population-based study of NAT2 indicated that the slow acetylation phenotype frequency varied based on race with approximately fourteen percent of Asians, thirty-four percent of Black Americans, and fifty-four percent White

---

<sup>50</sup>Esteban González Burchard et al., *The Importance of Race and Ethnic Background in Biomedical Research and Clinical Practice*, 348 NEW ENG. J. OF MED. 1170, 1172 (2003).

<sup>51</sup>American Lung Association, *Cystic Fibrosis (CF) Fact Sheet*, December 2004, available at <http://www.lungusa.org/site/pp.asp?c=dvLUK9O0E&b=35042#three>.

<sup>52</sup>Melanie Osby & Ira A. Shulman, *Phenotype Matching of Donor Red Blood Cell Units for Nonalloimmunized Sickle Cell Disease Patients: A Survey of 1182 North American Laboratories*, 129 ARCHIVES OF PATHOLOGY & LABORATORY MED. 190, 190 (2005).

<sup>53</sup>Burchard, *supra* note 50, at 1173.



possessing the slow acetylation phenotype.<sup>54</sup> The genetic variation of NAT2 between racial populations is important to establish as it may help doctors better predict differences in toxic effects of drugs based on race.<sup>55</sup> As these examples illustrate, race can be indicative of relative genetic risk of some diseases and response to drug treatment regimes.

While race can indicate genetic differences that will result in differential responses to drug treatments or susceptibility to disease, the genetic basis of drug response or disease susceptibility and the correlation with race is scientifically complex. Herein lies the problem—neither argument that race is meaningless or that race correlates with genetics with genetic traits—is completely correct. First, ancestry probably matters more than OMB defined race. Genetic variations among populations, for example racial populations, generally arise as the result of geographical isolation and limited admixture among members of the isolated populations. “Geographically localized populations clearly have different frequencies for many disease-related genetics variants.”<sup>56</sup> The primary point of scientific contention is whether race as defined by continental populations is a useful unit in assuming genetic similarity. Transfer of genetic variations among continental populations, which form the basis of the U.S. OMB racial classifications, historically has been limited by geographical distance based on sheer distance. In boundary areas, however, such as Northern and Eastern Africa, where there was more admixture of individuals from the European and African continent, the gene frequency in these populations does not easily fall into distinct Caucasian or Black categories.<sup>57</sup> For example, Ethiopians and Somalis “have greater genetic resemblance to Caucasians and are clearly intermediate between sub-Saharan Africans and Caucasians.”<sup>58</sup> Characterizing individuals of Ethiopian or Somalian descent as either Black or Caucasians fails to adequately take into account their genetic background. Similarly, these individuals will

---

<sup>54</sup>Mimi C. Yu et al., *Acetylator Phenotype, Aminobiphenyl-Hemoglobin Adduct Levels, and Bladder Cancer Risk in White, Black, and Asian Men in Los Angeles, California*, 86 J. OF NAT’L CANCER INST. 712, 712 (1994).

<sup>55</sup>Burchard, *supra* note 50, at 1173.

<sup>56</sup>Richard S. Cooper, *Race, Genes, and Health, New Wine in Old Bottles?*, 32 INT’L J. OF EPIDEMIOLOGY 23, 24 (2003).

<sup>57</sup>Genetic admixture of races has also been scientifically well documented in central Asia. See Burchard, *supra* note 50, at 1173.

<sup>58</sup>Risch, *supra* note 49, at comment2007.5.

likely show a genetic propensity for a disease or response to a drug treatment regime that cannot easily be classified as White or Black. This is but one example of countries with known admixture. While there are continental differences in allelic frequency, the use of race, particularly as articulated by OMB and utilized by the FDA, for individuals with ancestry from regions of the world with significant admixture response to drugs will similarly likely be intermediate and distinctly fall within racial classification.

Further, while geography often limits transfer of genetic variation among populations, there may also be other social or culture characteristics that limit admixture among groups within a single racial category. Ashkenazi Jews, for instance, are classified as Caucasian, but are genetically at higher risk for many diseases than the Caucasian population generally. This is likely because the population “descended from a relatively small number of founders and have remained endogamous for a large part of their history.”<sup>59</sup> For example, females possessing a mutation allele (BRCA1) in high-risk pedigrees have an 80-90% risk of developing breast cancer and a 40-50% risk of developing ovarian cancer over their lifetime.<sup>60</sup> The frequency of BRCA1 mutations is only 1 in 1666 in the general populations; however, women of Ashkenazi Jewish ancestry possess BRCA1 mutations at a frequency of 1 in 107.<sup>61</sup> As illustrated by the Ashkenazi Jews example, characterizing an individual as Caucasian without further analysis into the individuals sub-group ancestry will fail to acknowledge and treat potential medical risks because the use of race is both under and over-inclusive. This is but one example of how race fails to adequately approximate genetic risk. This likely does not represent an isolated case as “there can be considerable genetic heterogeneity within a [large geographical] region.”<sup>62</sup> Relying on the racial group to approximate the genotype is dangerous as it may not be an accurate statement.

---

<sup>59</sup>Burchard, *supra* note 50, at 1172.

<sup>60</sup>Jeffery P. Struwing et al., *The carrier frequency of BRCA1 185delAG mutation is approximately 1 percent in Ashkenazi Jewish individuals*, 11 NAT. GENETICS 198, 198 (1995).

<sup>61</sup>Lee, *supra* note 25, at 34.

<sup>62</sup>Sarah A. Tishkoff & Kenneth K. Kidd, *Implications of Biogeography of Human Populations for ‘Race’ and Medicine*, 36 NAT. GENETICS S21, S26 (2004).

Individuals whose genotype fails to correlate with the genotype of their racial group may be at risk for a disease or fail to take advantage of a drug treatment regime because they do not fit the genetic, racial stereotype. Race can be informative in a very crude manner as to the genetic propensity of an individual to develop a medical condition or response to a medical treatment, but there are also significant limitations as to the extent race is a proxy for genetic traits.

Secondly, the extent to which race should be relied upon by medical researchers and the FDA in approving race-specific drugs is further complicated by the problem of over and under inclusion of individuals in medical categories for disease susceptibility or drug response based on race. Genetic variation for complex disease is continuous, meaning that the phenotype variation resulting from genetic differences “among groups are graded, as opposed to dichotomous.”<sup>63</sup> Most diseases are not caused by a single mutation in one gene; rather the genetic basis of complex diseases such as heart disease, cancer, and diabetes are influenced by “a combination of polymorphisms in at least several genes, each of which has a small effect.”<sup>64</sup> For these type of complex diseases, disease susceptibility or drug response will not likely fall into two discrete categories, one “Black” and one “White.” Rather, the response will be graded because multiple genes and alleles of genes are contributing to the phenotypic effect. While the average disease susceptibility or drug treatment response for any racial group may be distinct, individuals regardless of race will likely vary along a phenotypic continuum. Some portion of the members of the racial group will inevitably fail to exhibit the stereotyped disease susceptibility or drug response resulting in over inclusion of individuals in a medical category based on race regardless of actual susceptibility or response. Further, there is the potential of under and over inclusion of individuals for genetic risk of disease or genetic appropriateness of treatment because of their

---

<sup>63</sup>Tate, *supra* note 4, at S37.

<sup>64</sup>Michael Bamshad et al, *Deconstructing the Relationship Between Race and Genetics*, 5 NAT. REVIEWS GENETICS 599, 607 (2004).

race. “Human populations differ from one another almost entirely in the vary proportions of the allelic genes of the various sets of hereditary factors, and not in the kind of genes they contain.”<sup>65</sup> The overall frequency of alleles in a racial population may vary among racial groups, but some individuals among racial population will share the same gene allele. “Membership in a genetically inferred cluster [i.e. racial group] does not mean that all members of the cluster necessarily have a similar genetic composition.”<sup>66</sup> Regardless of how the racial lines are drawn, race can only be a proxy for actual individual genotype. As a proxy, race will inevitably fail to include all members possessing a particular disease genotype and be over inclusive in some regards by including individuals who differ genetically with respect to the gene or genes of interest. All members of a race, however defined, are not genetically identical, and members of different races are not completely genetically different.

Most researchers recognize that race is merely a crude proxy for an individual’s actual genetic composition. Ideally, pharmacogenomics, an analysis of the correlation of an individual patient’s DNA sequence, rather than that of an ill-defined racial group, to response of drug treatment, should be utilized. Pharmacogenomics allows the “matching of medicines with the genetic makeup of an individual, to ensure use of medicines most likely to be effective and least likely to produce adverse drug reactions.”<sup>67</sup> In the realm of drug metabolism and cancer biology, pharmacogenomics has already shown great promise.<sup>68</sup> For example, the FDA has approved a pharmacogenomic drug, Herceptin®, which is a breast cancer treatment, on September 28, 1998.<sup>69</sup> Patients diagnosed with breast cancer are genetically screened to determine if they have a mutation resulting in over expression of the protein HER-2. Only patients over expressing HER-2 will be

---

<sup>65</sup>Morris W. Foster and Richard R. Sharp, *Race, Ethnicity, and Genomics: Social Classifications as Proxies of Biological Heterogeneity*, 12 GENOME RESEARCH 844, 844 (2002).

<sup>66</sup>Bamshad, *supra* note 64, at 607.

<sup>67</sup>Tate, *supra* note 4, at S38.

<sup>68</sup>Michelle Meadows, *Genomics and Personalized Medicine*, 39 FDA CONSUMER MAGAZINE (2005), at [http://www.fda.gov/fdac/features/2005/605\\_genomics.html](http://www.fda.gov/fdac/features/2005/605_genomics.html).

<sup>69</sup>See FDA, Trastuzumab, Genentech Herceptin Approval Letter (September 25, 1998), at [www.fda.gov/cder/foi/appletter/1998/trasgen0925981.pdf](http://www.fda.gov/cder/foi/appletter/1998/trasgen0925981.pdf) (last visited Mar. 28, 2006)

prescribed the drug, as Herceptin® is only effective in those patients.<sup>70</sup> The problem with pharmacogenomics and personalized medicine is that researchers need to know the molecular lesion(s) involved in the disease condition or that affects drug efficacy in order to implement the practice. “For complex diseases . . . , little progress has been made towards understanding any genetic basis within- or between-group variation.”<sup>71</sup> This is in part due to the fact that the ability of researchers “to predict accurately [complex traits] (even given genotypes for a subset of genes) is much lower than for more simply inherited traits.”<sup>72</sup> Actually knowing the particular disease gene responsible or that contributes to disease susceptibility or drug efficacy is a scientifically difficult and long process. Thus, race-based pharmacogenomics and diagnostics arise from “the fear that the promise of so-called personalized genetic medicine is increasingly unlikely to be fulfilled in the near-term future” and will prove a too costly research endeavor.<sup>73</sup> The scientific difficulty and cost in determining the gene of action associated with personalized medicine does not in itself justify the use of race as a crude marker for an individual’s genotype.

The fear of reliance upon race, rather than an individual’s genotype or even ancestry, is that society and the medical field will begin to see a disease as racialized and fail to promptly diagnosis or offer treatments to patients based on racial stereotypes. As discussed in this section, the ambiguous, genetically questionable reliance on continental racial categorization creates an issue of over and under-inclusion of individuals at genetic risk for a particular disease or potentially genetically responsive to a drug treatment regime. To illustrate these principles, take for example sickle cell anemia, a mutation in the  $\beta$ -globin gene. As previously mentioned, an African American newborn in the U.S. has a one in 500 chance of being affected by the disease.<sup>74</sup> African-Americans have a high risk of being born with sickle cell anemia; however, sickle cell

---

<sup>70</sup>See Michael B. Losow, *Personalized Medicine & Race-Based Drug Development: Addressing Minority Health Care Disparities In An Ethically Charged Area*, 20 ST. JOHN’S J. LEGAL COMMENT. 15, 21 (2005).

<sup>71</sup>Joanna L. Mountain and Neil Risch, *Assessing Genetic Contributions to Phenotypic Differences Among ‘Racial’ and ‘Ethnic’ Groups*, 36 NAT. GENETICS S48, S51 (2004).

<sup>72</sup>*Id.* at S52.

<sup>73</sup>C. Condit and B. Bates, *How Lay People Respond to Messages about Genetics, Health, and Race*, 68 CLINICAL GENETICS 97, 98 (2005).

<sup>74</sup>See Osby & Shulman, *supra* note 52, at 190.

anemia affects not only member of the Black racial group and does not affect all Blacks equally. Blacks from southern regions of the African continent generally do not carry the genetic mutation associated with sickle cell anemia.<sup>75</sup> Further, while the rate of sickle cell anemia is extremely low in Caucasians and Asians generally, sickle cell anemia is relatively common among people with ancestry from Mediterranean countries such as Greece and Turkey and the Asian country, India.<sup>76</sup> Viewing sickle cell anemia as a Black disease is dangerous in that patients who do not fit the racial categorization associated with the disease may be misdiagnosed and not get timely treatment.<sup>77</sup> Sickle cell anemia is genetically relatively easily identified as the disease is caused by a point mutation in a single gene. “Once the affected gene is known, anybody can be tested for the disease causing mutation. Race becomes irrelevant.”<sup>78</sup> Color-blind genetic testing of infants, which is universally required in 49 of the 50 states for sickle cell, can detect sickle cell anemia early minimizing the risk of misdiagnosis based on racial stereotypes.<sup>79</sup> For many diseases, genetic testing is not possible as multiple genes may contribute to the risk of the disease or the molecular lesion(s) associated with the disease are unknown. Thus, patients rely upon medical expertise to ensure that are correctly diagnosed and properly treated. The FDA should proceed cautiously in approving race-specific drugs as creation of racially specialized drug treatments or indirectly the development of racialized diseases has the potential to delay both diagnosis and treatment of patient relying on the FDA to ensure the safety and efficacy of drugs.

### ***Race and Environment***

<sup>75</sup>See Rotman, *supra* note 12. Most African-Americans have ancestry that migrated to the United States from West Africa as a result of the slave trade in early America. See Bamshad, *supra* note 64, at 605.

<sup>76</sup>See Schwartz, *supra* note 42, at 1393; see also D. Mohanty & M.B. Mukherjee, *Sickle Cell Disease in India*, 9 CURRENT OPINION HEMATOLOGY 117, 117 (2002).

<sup>77</sup>See Frank E. Shafer et al., *Newborn Screening for Sickle Cell Disease: Four Years of Experience from California's Newborn Screening Program*, 18 J. PEDIATRIC HEMATOLOGY ONCOLOGY 36, 36 (1996) (“The prevalence and ethnicity data presented here [in the study] demonstrate the ineffectiveness of targeted screening [based on race or ethnicity] and justify universal screening.”)

<sup>78</sup>Gregory A. Petsko, *Color Blind*, 5 GENOME BIOLOGY 119, 120 (2004).

<sup>79</sup>National Newborn Screening and Genetics Resource Center, *National Newborn Screening Status Report: U.S. National Screening Status Report Updated 03/03/06*, at <http://genes-r-us.uthscsa.edu/nbsdisorders.htm> (last visited Mar. 25, 2006).

Racial differences in drug response and disease symptoms will likely be significantly influenced by environmental factors that are not innate or represent a genetic predisposition. Epidemiologically, reporting and understanding environmental factors with a higher prevalence in some racial groups and the correlation with disease severity is important in improving the health of affected individuals. Epidemiological studies have indicated that risk factors and behaviors are often “associated with both race or ethnicity and health outcomes[,]” which may explain some of the racial health disparities.<sup>80</sup> For example, one research study “found that six well-established risk factors (tobacco use, hypertension, hyperlipidemia, alcohol intake, excess weight, and diabetes mellitus) accounted for 31% of the excess mortality between Black and White adults.”<sup>81</sup> Racial differences, whether the result of genetics or environment, represent real difference in susceptibility to disease and potential response to a drug treatment regime.

While the racial difference in disease susceptibility or drug treatment efficacy, the FDA should be hesitant to approve race-specific drugs where the differences between racial populations is likely the result of environmental factors, rather than genetic differences among races. Potentially efficacious drugs will likely be denied to individuals based on race even though they share similar socio-economic and environmental risk factors that form the underlying basis of the racially differential effect. Research indicates that “[c]ommon diseases result from complex interactions between genetic and environmental factors.”<sup>82</sup> Thus, even if an individual possesses a gene associated with a disease, the patient will not necessarily develop the disease or the severity disease symptoms will often depend on environmental factors. The significant environmental contribution to disease risk complicates the use of race as a proxy for an individual’s genetic composition. As one researcher indicated “[t]he problem is that an individual’s response to a drug depends on a host of factors, including overall health, lifestyle, support system, education, and socioeconomic status—all of

---

<sup>80</sup>Mays, *supra* note 22, at 86.

<sup>81</sup>*Id.*

<sup>82</sup>Tate, *supra* note 4, at S38.

which are . . . likely to be affected, at least in the United States, by a person's race."<sup>83</sup> While admittedly researchers cannot control for every environmental factor, the FDA drug approval of race-specific drugs is particularly problematic as race as seen by many particularly in the general public as a proxy for innate genetic differences, which can entrench discriminatory racial stereotypes and race division, rather than merely environmental differences. Any racial differences that researchers find in occurrence rates of diseases or drug responses may not be the result of some inherent genetic difference between racial populations, but partially the result of environmental factors. For example, within the African American population, darker-skinned Blacks generally have higher blood pressure than lighter-skinned Blacks.<sup>84</sup> This difference in mean blood pressure is not the direct result of skin color per se. Rather, according to researchers, "the association was dependent on socioeconomic status, whether measured by education or an index consisting of education, occupation, and ethnicity[.]"<sup>85</sup> Lower socioeconomic status correlated with darker skin color as "darker skin color in the United States is associated with less access to scarce and valued resources of the society."<sup>86</sup> Environmental factors, often associated with socioeconomic status and in part the product of racism, can significantly influence susceptibility to disease and drug treatment response.

To further illustrate the environmental contribution to disease, consider the disease, Asthma. The rate of asthma in Black populations and White populations differs by less than two percent.<sup>87</sup> According to the Center for Disease Control, however, Blacks are approximately three times more likely to be hospitalized and die from Asthma than Whites.<sup>88</sup> "These disease rate differences are of an entirely different magnitude from those associated with potential genetic differences between two populations, suggesting etiologies due to

---

<sup>83</sup>Anonymous, *Genes, drugs, and race*, 29 NAT. GENETICS 239, 240 (2001).

<sup>84</sup>Duster, *supra* note 13, at 1051.

<sup>85</sup>M.J. Klag et al., *The Association of Skin Color with Blood Pressure in US Black with Low Socioeconomic Status*, 265 J. OF AM. MEDICAL ASSOC. 599, 599 (1991).

<sup>86</sup>Duster, *supra* note 13, at 1051.

<sup>87</sup>See L. Rhodes et al., *Asthma Prevalence and Control Characteristics by Race/Ethnicity—United States, 2002*, 53 MORBIDITY & MORTALITY WEEKLY REPORT 145, 146 (2004) (7.6% of White, non-Hispanic reporting current Asthma compared to 9.3% of Black, non-Hispanic).

<sup>88</sup>See *id.* at 147; see also Arialdi M. Miniño et al, *Deaths: Final Data for 2000*, 50 NAT'L VITAL STATISTICS REPORT 1, 60 (2002) (death rate of 1.3% of Whites compared to 3.9% of Blacks).



environmental differences of toxic exposures, housing quality, and access to health care.”<sup>89</sup> Thus, the severity of asthma symptoms likely correlates with environmental factors that are more prevalent within certain racial populations. As one researcher noted that for numerous complex genetic diseases, “many differences in drug response associated with race or ethnicity are due to environmental correlates rather than population genetic differences.”<sup>90</sup> There is a recognition in the field of epidemiology that environment is making a significant contribution to disease progression, and the goal of the research is to identify those environmental factors. While the environmental risk factors may initially be identified in one racial category the finding of environmental risk are applicable to anyone regardless of race in a similar environment. However, when a drug company seeks and the FDA approves a drug for use in discrete racial populations, the FDA and drug manufacturer are saying that there are innate difference between races, differences at the level of an individual’s DNA. The racial differences in response to a drug could be 80% environmental (the FDA and drug manufacturer would not know because there is no requirement to distinguish between environmental and genetic contribution to the racial difference in drug response), but when the FDA approves the drug for use in a single racial group, those who potentially could benefit as they are exposed to similar environmental factors will be denied unless a doctor chooses to prescribe the drug off-label.<sup>91</sup>

Some will argue that even if the racial differences in drug response or disease progression and severity are the result of environmental factors, likely significantly influenced by socioeconomics and racial discrimination, the FDA approval of race-specific drugs is justified because regardless of cause, there are undeniable differences in general between races. In regards to socioeconomic environmental factors, the problem is and “[i]t is important to emphasize that race and ethnicity are distinct from socioeconomic status (i.e. income, edu-

---

<sup>89</sup>Jacqueline Stevens, *Racial Meanings and Scientific Methods: Changing Policies for NIH-Sponsored Publications Reporting Human Variation*, 28 J. of HEALTH POLITICS, POLICY & LAW 1033, 1069 (2003).

<sup>90</sup>Tate, *supra* note 4, at S37.

<sup>91</sup>See Krauss, *supra* note 12.

cation, and occupation).”<sup>92</sup> Minorities do disproportionately represent the lower levels of the United States socioeconomic stratus. According to the 200 Census, approximately 22% of Blacks and 21% of Hispanics were below the poverty line while only 9.4% of Whites (7.5% of White, Non-Hispanics) were below poverty levels.<sup>93</sup> However, when one looks at the individuals behind the percentages, while approximately 7,900,000 Blacks and 7,155,000 Hispanics were below the poverty line, so too were 21,291,000 Whites (14,572,000 White, Non-Hispanics).<sup>94</sup> Socioeconomic status is “a robust predictor of access to and quality of health care and education.”<sup>95</sup> Environmental factors associated with poverty are not the result of genetics and knows no racial lines. If the FDA approves race-specific drugs where environmental factors, particularly environmental factors associated with socioeconomic status, form the basis for racial differences, the FDA significantly impedes the ability of other individuals in similar environmental situations to obtain efficacious drug treatments. Race may be a “quick and dirty way” of addressing environmental influences on drug response or disease progression, but left behind are the potentially millions of other similarly situated, racially different individuals, who will be delayed and/or potentially foreclosed access to helpful treatment regimes. The FDA should proceed judiciously when considering the approval of race-specific drugs and advocate for an extremely limited use of race only upon showing of a scientific basis and necessity because racial differences in drug response may in large part be the result of socioeconomic environmental factors, rather than genetics differences, that know no race.

### ***Race, Medicine, and Discrimination***

---

<sup>92</sup>Jamie M. Doyle, *What Race and Ethnicity Measure in Pharmacologic Research*, 46 J. OF CLINICAL PHARMACOLOGY, 401, 401 (2006).

<sup>93</sup>JOSEPH DALAKER, U.S. CENSUS BUREAU, POVERTY IN THE UNITED STATES: 2000, P60-214 CURRENT POPULATION REPORTS 2 (Sept. 2001), *available at* [www.census.gov/prod/2001pubs/p60-214.pdf](http://www.census.gov/prod/2001pubs/p60-214.pdf).

<sup>94</sup>*Id.*

<sup>95</sup>Burchard, *supra* note 50, at 1171.

Race is a contentious concept within society that often results in discrimination even in the arena of health care access and medicine. “It is indisputable that social perceptions of what a person is or is not [racially] influences the availability, delivery, and outcome of medical care.”<sup>96</sup> Based on race, “a physicians’ perception of and interactions with a patient may differ[.]”<sup>97</sup> As a result, “[s]ignificant disparities exist in health status, health care utilization, and outcomes among different racial and ethnic groups.”<sup>98</sup> Even when patient, who is a member of a minority racial group, has the same insurance coverage plan as a white patient, generally the minority patient will receive fewer doctor visits, receive less primary care services, and less preventative procedures.<sup>99</sup> African-Americans upon hospitalization will receive “fewer surgical interventions, diagnostic tests, medical services, and less optimal interventions than whites—even when their diagnosis, symptoms, and source of payment are the same.”<sup>100</sup> Particularly as these facts indicate there is a “synergistic combination of minority status and social class significantly impedes improvements in health outcomes among racial and ethnic minorities in the United States.”<sup>101</sup> Minority racial groups disproportionately are represented in the low echelons of the socioeconomic strata, as a result exposed to many negative environmental health factors associated with poverty, and the risk of increased severity and prevalence of disease is only exacerbated by racism. Racial discrimination exists and is a problem within the medical health care industry. The use of race in the FDA approval process may be important to ensure the health care needs of minority U.S. racial populations are being met. “Although race or ethnicity, per se, is not casual, it may still function as a risk indicator providing some reduction in uncertainty about the likelihood of morbidity or mortality.”<sup>102</sup> Race may serve as an important crude indicator that allows physicians to better address the needs of their

---

<sup>96</sup>Schwartz, *supra* note 42, at 1392.

<sup>97</sup>Andrew J. Karter, *Commentary: Race, Genetics, and Disease—In Search of a Middle Ground*, 32 INT’L J. OF EPIDEMIOLOGY 26, 27 (2003).

<sup>98</sup>Lea Harty et al., *Race and Ethnicity in the Era of Emerging Pharmacogenomics*, 46 J. OF CLINICAL PHARMACOLOGY 405, 405 (2006).

<sup>99</sup>Sidney D. Watson, *Race, Ethnicity and Quality of Care: Inequalities and Incentives*, 27 AM. J.L. & MED. 203, 205 (2001).

<sup>100</sup>*Id.* at 206.

<sup>101</sup>Doyle, *supra* note 92, at 401.

<sup>102</sup>Mays, *supra* note 22, at 85.

patients. Further, as racial and ethnic minorities are often underrepresented in clinical trial, most drugs are tested for safety and efficacy on primarily white individuals.<sup>103</sup> By impose additional regulations regarding the use of race in the FDA approval process, one could argue that manufacturers will be less likely to investigate racial differences in disease and drug treatment efficacy. Thus, factors result in racial differences in disease or drug response, whether race specific or not, will never be identified.<sup>104</sup> In addition, clinical data regarding disease and drug treatments in minority U.S. racial subpopulations may be relevant in addressing the medical needs of individuals who are of similar racial backgrounds in developing countries.<sup>105</sup> There is a legitimate argument that the FDA approval of race-specific drugs could be important in minimizing racism and ensuring that drugs that are safe and effective for minority racial groups.

While a legitimate argument can be made to not impose additional restrictions on FDA approval of race-specific medicines, because of the potential for promoting racial discrimination and stereotyping, FDA should further limit the FDA approval of race-specific drugs to instances where there is a clear scientific basis and necessity particularly. While there is a history of inferior health care for minority races in the United States, the FDA approval of race-specific drugs will not likely end racism within the scientific communities, but only exacerbate the racial divide. The fear is that race-based medicines will lead to racial discrimination and exacerbate racial disparities in medical care in three ways: (1) “heighten attention to biological differences between groups by physicians,” (2) “increase the relatively high levels of distrust minorities already hold toward the medical profession,” and (3) further entrench racial stereotypes and discrimination of the general public by heightened attention to putative biological differences between races.<sup>106</sup>

The fear of increased racial disparities in health care by physicians based upon heightened attention to biological differences is not unfounded. The scientific and medical communities are not immune to the problems

---

<sup>103</sup>See Burchard, *supra* note 50, at 1174.

<sup>104</sup>*Id.*

<sup>105</sup>See Abdallah S. Daar & Peter A. Singer, *Pharmacogenetics and Geographical Ancestry: Implications for Drug Development and Global Health*, 6 NAT. REV. GENETICS 241, 244 (2005).

<sup>106</sup>Condit, *supra* note 73, at 98.

of race discrimination. The classic examples are the eugenics movement in the United States and around the world and Holocaust in Nazi Germany. When the FDA approves a race-specific drug, the FDA is saying, whether intentional or not, that a drug works for one racial group of people and not another. The FDA is saying that there are fundamental, innate biological differences between the races in regards to efficacy and safety of a new drug. This is in spite of the lack of knowledge as to the true underlying cause of the disease—proportional racial differences in environmental factors, genetic factors, or some combination of both that result in the racial disparity in drug effect.<sup>107</sup> Doctors and other members of the medical community relying upon the legislatively mandated role of the FDA in ensure only safe and effective new drugs are approved for public marketing will rely on the FDA-approved product insert indicating race-specific prescription of the drug.<sup>108</sup> Different drug treatment regimes will be initiated based on race, a concept, as has already been discussed in previous sections, of questionable scientific relevancy and validity in drug treatment. This leads to “an easy slide down the slope to the misconceptions of “Black” or “White” diseases[,]” regardless of whether the disease actually effects members of multiple racial groups or the drug could benefit members of multiple racial populations.<sup>109</sup> The FDA approval of race-specific drugs reinforces the notion that races are inherently different and has the potential for further widening of the medical services gap between some minority races and Whites.

The FDA approval of race-specific drugs could further entrench the distrust of some minority racial populations feel towards the medical profession.<sup>110</sup> Research studies indicate that minority trust in medical research

---

<sup>107</sup>One could similarly argue that the FDA approval of drugs based on gender carries the same potential for discrimination based on public perception of innate biological differences and therefore, FDA approval and clinical testing on women as a subgroup population should be limited. A key distinction, however, is that the terms male and female are not merely social constructs, but are recognized by the scientific community to have a biological basis that result in innate physiological differences. *See, e.g.* David D. Federman, *The Biology of Human Sex Differences*, 354 NEW ENG. J. OF MED. 1507 (2006). Unlike gender, race as discussed in previous section has debatable and limited scientific legitimacy as a term denoting biological and physiological differences.

<sup>108</sup>*See* 21 U.S.C. § 355(d) (2004).

<sup>109</sup>Duster, *supra* note 13, at 1051.

<sup>110</sup>Sharona Hoffman, “Racially-Tailored” Medicine Unraveled, 55 AM. U. L. REV. 395, 426 (2005); *but see* Wendler, *supra* note 14, at 7 (indicating that willingness to participate in medical trials was not the result of distrust of the medical profession, but rather “substantial differences by race and ethnicity in the number of individuals *invited* to participate’ by medical researchers) (emphasis in original text).

and the medical profession generally, have been undermined by historic abuses like the Tuskegee syphilis trials where African-Americans were not treated with available antibiotics known to cure the disease, but instead allowed to progress to end-stage syphilis disease symptoms.<sup>111</sup> The approval of race-specific drugs does not quell minority distrust of the medical industry. According to one research survey, when asked “How suspicious would you be that a drug designated as preferred for African-Americans was not as safe as a drug designated as preferred for European-Americans?”, 53% of African-American and 49% of all respondents said they would be ‘very suspicious.’ Only 12% of both sets of respondents said that they would be ‘not suspicious.’<sup>112</sup> In another study, after being asked to read a print message about a hypothetical drug, ‘Fairdil,’ which stated that people of European and African ancestry may have different responses to heart medication and that “Fairdil has been shown to be more effective for more African Americans in treating high blood pressure”, only 20% of lay participants believed the message.<sup>113</sup> The FDA approval of race-based drugs may increase minority suspicion of the medical community and only intensify the disparity between the races in regards to health care services.

Finally, the FDA approval of race-specific drugs may serve only to further entrench the inequity of medical treatment and generally racial inequality in the United States society by heightening the attention of the lay public to putative biological differences between races. When scientist report or, in particular, when the FDA approves a drug advocating race-specific results without investigating further the basis of the racial disparity in drug response, i.e. environmental or genetic factors, there is the potential that members of the scientific and medical communities, and the public generally, will engage over in genetic reductionism. “Public perception that scientific evidence has established that a particular ‘race’ is more vulnerable to life-threatening illnesses than others or does not respond to medications that cure most patients may reinforce

<sup>111</sup> See Giselle Corbie-Smith et al., Distrust, Race, and Research, 162 ARCHIVES OF INT’L MEDICINE 2458, 2458 (2002).

<sup>112</sup> Condit, *supra* note 73, at 100 (quoting C.M. Condit et al., *Exploration of the Impact of Messages about Genes and Race on Lay Attitudes*, 66 CLINICAL GENETICS 402 (2004).

<sup>113</sup> *Id.* at 101 (quoting B.R. Bates et al., *Evaluating Direct-to-Consumer Marketing of Race-based Pharmacogenomics: A focus Group Study of Public Understanding of Applied Genomic Medications*, 9 J. OF HEALTH COMMUN. 541 (2004))

negative 'race-based' stereotypes and misconceptions. Particular populations may be seen as diseased or incurable."<sup>114</sup> This can lead to stigmatization not only in the general public, both also at the office and in regards to procuring health and/or life insurance. Employers and insurers may discriminate based upon lower potential employee productivity because of absences or require a higher premium to be paid based on the racial population an individual belongs to regardless of whether the individual is actually predisposed to a disease or will respond to treatment. Mere membership in the larger racial group will result in the individual patient having their health risk stereotyped. "There is a tendency for scientists to ignore the messy social implications of what they do."<sup>115</sup> However, there are undeniable series implications regarding the potential for racial discrimination that the FDA, as an agency possessing scientific and policy expertise, should consider before continuing down the path to further approvals of race-specific drugs.

### ***Legal Authority***

As advocated throughout this paper, when considering the approval of race-specific drugs, the FDA should implement a public policy with an extremely limited use of race only upon showing of scientifically significant data demonstrating a racially differential effect and the need to rely on race in the absence of any other available population markers. However, a fundamental question remains of whether the FDA is legally authorized in withholding new drug application approval based on failure to present data showing a racially differential effect of the drug. While the FDA generally has considerable agency discretion in creating regulatory policy through both the text of the organic agency statute and the Administration Procedure Act, a strong argument can be made that the FDA lacks the statutory basis for authority to require manufacturers undertake clinical trials to show statistically significant data demonstrating a racially differential effect.

---

<sup>114</sup>Hoffman, *supra* note 110, at 423.

<sup>115</sup>Richard S. Cooper et al, *Race and Genomics*, 348 NEW ENG. J. OF MED. 1166, 1169 (2003).

The basis for the argument that the FDA cannot impose restrictions on the use of race during the FDA approval process is based on the reasoning in the district court decision in *Ass'n of American Physicians and Surgeons, Inc. v. United States Food and Drug Administration*.<sup>116</sup> In the case, the FDA regulations “requiring drug manufacturers to conduct drug tests on pediatric populations and suggest pediatric doses for drugs,” even though the drugs were intended for adult populations, was challenged as exceeding the FDA’s congressional grant of authority and being arbitrary and capricious.<sup>117</sup> The district court ruled that the pediatric regulation exceeded FDA’s statutory authority. In reaching this decision, the district court found the labeling provisions 21 U.S.C. §§ 352(a), 352(f), 355(d)(7), and 321(n), requiring the labeling to reveal material “facts . . . under such conditions of use as are customary or usual,” did not vest the FDA with the power to promulgate the Pediatric Rule.<sup>118</sup> The court focused on the language “customary or usual” in the text of the statute and indicated that new drugs “do not have any customary or usual use,” so this does not establish a clear basis for the Pediatric Rule.<sup>119</sup> The FDA also relied upon 21 U.S.C. §§ 321(p), 331(a) and (d) and 355 (a), (j), and (d), which requires the manufacturer of a new drug to demonstrate that the product is safe “for use under the conditions prescribed, recommended, or suggested in the purposed labeling thereof.”<sup>120</sup> The court disagreed with the FDA’s reliance on §§ 355(d) and 321(p) indicating that the Pediatric Rule goes beyond the statutory requirement by requiring “manufacturers to test products for use on children, even if such a use is not prescribed, recommended, or suggested by the products’ label.”<sup>121</sup> Finally, the court addressed whether the Pediatric Rule promulgated “fit[s] into the overall regulatory scheme created by Congress.”<sup>122</sup> The court reasoned that if Congress enacted a distinct regulatory scheme on the given issue, “Congress demonstrates its intention to occupy the field, and any attempt by the FDA to inter-

---

<sup>116</sup>226 F.Supp.2d 204 (D.C. 2002).

<sup>117</sup>*Id.* at 204.

<sup>118</sup>21 U.S.C. § 321(n)

<sup>119</sup>*Ass’n of Am. Physicians & Surgeons*, 226 F.Supp.2d at 214.

<sup>120</sup>*Id.*

<sup>121</sup>*Ass’n of Am. Physicians and Surgeons*, 226 F.Supp.2d at 215.

<sup>122</sup>*Brown & Williamson Tobacco Corp. v. FDA*, 153 F.3d 155, 163 (4th Cir. 1998) *aff’d* 529 U.S. 120 (2000).



vene with an inconsistent regime shall be deemed in excess of its authority.”<sup>123</sup> The court found that the passage of the Best Pharmaceuticals for Children Act (BPCA), Congress expressed its intent to occupy the field.<sup>124</sup> Further, the BPCA and the FDA’s Pediatric Rule, according to the court, are incompatible because “the very thrust of the BPCA—providing marketing incentives to encourage voluntary testing—is entirely anomalous with the very thrust of the Pediatric Rule—requiring such tests in the absence of a deferral or waiver.”<sup>125</sup> For the foregoing reasons, the district court found the FDA exceeded its authority by promulgating the Pediatric Rule requiring drug manufacturers to test on pediatric populations.<sup>126</sup>

The *Ass’n of American, Physicians and Surgeons* case calls into question the ability and authority of the FDA to require clinical data indicating a clear scientific basis and necessity for the reliance on race. First, one should note that *Ass’n of American, Physicians and Surgeons*, the district court indicated the question of whether the FDA had authority to require pediatric drug testing “is a close one[.]”<sup>127</sup> Further, the “opinion was the work of a lone district court judge.”<sup>128</sup> Based on public policy and the broad statutory language of the Federal Food, Drug, and Cosmetic Act (“FDCA”), one could argue that *Ass’n of American, Physicians and Surgeons* was wrongly decided. The FDA should be allowed to require clinical testing in special populations as a condition for FDA approval subject to review under an arbitrary and capricious standard. Alternatively, one could argue that the *Ass’n of American, Physicians and Surgeons* decision in the context of pediatric drugs is distinguishable from the context of race-based drugs. However, the case advocating for the ability of the FDA to regulate the use of race and requiring clinical trial data showing a differential racial effect of drugs to support the use of race in labeling is stronger than in the pediatric

---

<sup>123</sup>*Ass’n of Am. Physicians and Surgeons*, 226 F.Supp.2d at 219.

<sup>124</sup>*Id.* at 221.

<sup>125</sup>*Id.*

<sup>126</sup>*Id.* at 222.

<sup>127</sup>*Id.* at 213.

<sup>128</sup>Charlie Steenberg, *The FDA’s Use of Postmarketing (“Phase IV”) Study Requirements: Exception to Rule and Promise to Problem* at 107 (2005), in Peter Barton Hutt, ed., *Food and Drug Law: An Electronic Book of Student Papers*, available at <http://leda.law.harvard.edu/leda/search/toc.php3?handle=HLS.Library.Leda/steenburgc-fdas-use-postmarketing>.

drug context. While beyond the scope of this paper, there are credible arguments, not presented in *Ass’n of American, Physicians and Surgeon*, that the FDCA empowers the FDA to require testing in subpopulations not mentioned in its labeling, or even disclaimed, under § 502(f) and (k).<sup>129</sup> Further, the decision in *Ass’n of American, Physicians and Surgeon* “turned at least in part on the tension between the pediatric rule’s mandatory requirements for pediatric studies and the [BPCA’s] incentive-laden scheme for encouraging them.”<sup>130</sup> Unlike in the context of pediatric drugs, Congress has not explicitly expressed its intent to regulate race-specific drugs. No marketing incentive similar to the BPCA has been proposed by Congress to incentivize manufacturers to test drugs in specific racial populations. As a part of the Food and Drug Modernization Act (FDMA) of 1997, Congress amended § 355(b)(1) to include the language, “The Secretary shall . . . review and develop guidance, as appropriate, on the inclusion of women and minorities in clinical trials . . . .”<sup>131</sup> Thus, contrary to the FDA requirements for pediatric trials, Congress has not developed a specific scheme to monitor the use of race in clinical trials as in the case of BPCA. The text of the statute grants authority to the FDA to issue guidance related to the inclusion of minorities. Further, while Congress did not specifically delegate authority to the FDA to regulate the inclusion of minorities based on the text of FDMA, neither does the statute prohibit the FDA from developing regulations regarding race-specific drugs to the FDA. *Ass’n of American, Physicians and Surgeon* does not unequivocally foreclose the ability of the FDA to offer policy guidance and regulate the use of race and prose clinical testing requirements when race is used, but the extent of FDA’s legal and statutory authority to promulgate clinical testing requirements is questionable and debatable.

Also, unlike in the context of pediatric drugs, the use of race in clinical trials and in the context of FDA drug

---

<sup>129</sup>*Id.*; See, e.g. Derek Ho, Adopting the Therapeutic Orphan? A Legal and Regulatory Assessment of the FDA’s Pediatric testing Rule (2000), in Peter Barton Hutt, ed., *Food and Drug Law: An Electronic Book of Student Papers*, available at [http://leda.law.harvard.edu/leda/search/toc.php3?handle=HLS.Library.Leda/hod-adopting.therapeutic\\_orphan](http://leda.law.harvard.edu/leda/search/toc.php3?handle=HLS.Library.Leda/hod-adopting.therapeutic_orphan).

<sup>130</sup>Steenberg, *supra* note 128, at 107.

<sup>131</sup>Admittedly, the statutory language “inclusion of women and minorities” is ambiguous in respect to whether “minorities” are to be treated as a single class or distinct racial classes.

approval raises serious potential Equal Protection Clause issues under the Fourteenth Amendment of the U.S. Constitution. The Equal Protection Clause provides that no state shall “deny to any person within its jurisdiction equal protection under the law.”<sup>132</sup> The Supreme Court has indicated that “racial classifications imposed by the government must be analyzed by a review court under strict scrutiny” and “such “classifications are constitutional only if they are narrowly tailored to further a compelling government interest.”<sup>133</sup> Some commentators have contended that the FDA is legally prohibited from approving race-specific drugs and argued the viability of the Equal Protection Clause and a number of federal anti-discrimination provisions that could be violated by the FDA approval of race-based medicines.<sup>134</sup> While I disagree that the use of race in the FDA approval process is *per se* unconstitutional and recognize that the text of the FDCA on its face is unconstitutional, one could argue that the application of FDA approval authority of race-specific drugs under §355(c) and (d) is government action utilizing race and thus subject to strict scrutiny analysis. In order for the FDA action and the use of race in drug approval to be found constitutional under the Equal Protection Clause of the U.S. Constitution, there must be a compelling government interest and the use of race must be narrowly tailored.<sup>135</sup>

While the health and safety of racial subpopulations is a compelling government interest, it is unclear if the FDA has met the second requirement of the Equal Protection Clause analysis—the narrow tailoring requirement. The purpose of the narrow tailoring requirement “is to ensure that the means chosen fit the compelling goal so closely that there is little or no possibility that the motive for the classification was illegitimate racial prejudice or stereotype.”<sup>136</sup> As people are being potentially denied life saving drugs based on race unless doctors know that the drug may be effective in other races and is willing to prescribe the drug

---

<sup>132</sup>U.S. Const. Amend. 14, §2.

<sup>133</sup>Grutter v. Bollinger, 539 U.S. 306, 326 (2003).

<sup>134</sup>For an excellent and insightful review of potential federal causes of action in regards to race-specific medicines, i.e. Constitutions Equal Protection Clause, 42 U.S.C. §1981, and Civil Rights Act of 1964, see Lillquist, *supra* note 13, at 442-466.

<sup>135</sup>See Grutter, 539 U.S. at 327.

<sup>136</sup>*Id.* at 333.

off-label, the automatic FDA approval of drugs for uses and indications within specific racial populations without a showing of any statistically significant data indicating the need to rely on the proposed racial distinction could be argued to violate the Equal Protection Clause by failing to meet the narrowly tailored requirement. The FDA arguable is required to preserve the constitutionality of its race-specific drug approval actions by narrowly tailoring the use of race. As such, one could argue that limiting the approval of new drug application targeted to specific racial population to situations where there is a clear scientific basis for the reliance on race and necessity as shown by the lack of any other known, correlating clinical markers is required to ensure the FDA does not violate the Equal Protection Clause.

The legal statutory and constitutional legitimacy and authorization of the FDA to require drug manufacturers to show a scientific basis for the reliance on race is debatable. To clearly resolve this issue without litigation, congressional action may be required to establish a framework to guide the FDA in its approval of race-specific medicines or to specifically grant authority to the FDA to develop race specific drugs. Interestingly, in the context of pediatric drugs, after *Ass'n of American, Physicians and Surgeon*, a group of Senators “savaged” the *Ass'n of American, Physicians and Surgeon* decision as “ill-considered and obviously errant.”<sup>137</sup> Further, the case resulted “in the 2003 PREA, which clearly authorized certain Phase IV studies by giving the power to require (and defer) pediatric trials in limited circumstances.”<sup>138</sup> The foregoing describes the potential limitations and legal issues surround the FDA’s congressionally delegated authority to require statistically significant data showing race differential effects. However, based on the statutory distinctions between pediatric drugs and race-specific drugs and the U.S. Constitution Equal Protection Clause arguments, there is a reasonable legal basis for requiring drugs a clear scientific basis for the reliance on race, such as data indicating racially different responses to a drug, before drugs are approved to be marketed and used in racial subpopulations.

---

<sup>137</sup>Steenberg, *supra* note 128, at 107.

<sup>138</sup>*Id.*

## *Recommendations*

The FDCA vests in the Secretary of Health and Human Services, who operates through the FDA, authority to approve new drugs.<sup>139</sup> Pursuant to the FDCA, drug manufacturers are required to receive premarket approval of candidate drugs by submitting a full report showing that the drug is safe and effective for the intended use.<sup>140</sup> The FDA drug approval process serves as the gatekeeper to ensure that safe and effective drugs are made available to the United States public regardless of race. Recognizing that there may be some biological relevance to racial categorization and current general infeasibility of pharmacogenomics, I would advocate for the FDA to narrowly tailor the use of race and limit race-specific claims in FDA drug approval to situations in which there is a clear scientific basis and necessity for the reliance on race. The FDA could evaluate the scientific basis and necessity of race by utilizing scientific advisory panels pursuant to 21 U.S.C. § 355(n), who based on the evidence presented at the drug approval process and their scientific expertise could access these criteria. Any racial disparity would need to be shown on a statistically significant patient population.<sup>141</sup> Further, the term race, as utilized in any clinical trial, and the manner in which patient participants were classified in regards to race should be clearly defined.

As an example of how review of a drug application for a race-specific medicine would occur using the narrowly tailored recommendation consider the case of BiDil®. Applying the requirements for statistically significant clinical data demonstrating racial differences and the necessity to rely on race as a marker, BiDil® would still be approved by the FDA. Clinical testing of BiDil® in a mixed-population (primarily white) revealed therapeutic differences that were only of border-line statistical significance in the first trial.<sup>142</sup>

---

<sup>139</sup>See 21 U.S.C. § 371 (2004).

<sup>140</sup>See 21 U.S.C. § 355(d) (2004),

<sup>141</sup>Under the current FDA guidelines, the racial and ethnic identity of clinical trial participants is to be recorded but there is no requirement that there be statistically significant numbers of any racial group participating in the clinical trial. See FDA, *supra* note 17. While beyond the scope of this paper, the mere requirement of reporting subpopulation identity without requiring statistically significant numbers of individuals from any one subpopulation does not allow for scientific conclusions to be drawn comparing races because any race-specific data generated from the trial may not be statistically significant.

<sup>142</sup>Kahn, *supra* note 5, at 12. Please note that in the second clinical trial, there were too many variables in the protocol at

When tested on self-identified Blacks, the efficacy of the drug was statistically significant.<sup>143</sup> Therefore, BiDil® manufacturers have demonstrated that there is a scientific basis for the use of race as evident by the racial differences in drug response. In regards to the second prong of the narrowly tailored use of race recommendation, necessity for reliance on race, there is speculation that the efficacy of BiDil® in Blacks is based on a nitric oxide deficiency.<sup>144</sup> While there is speculation that nitric oxide levels could serve as a non-racial marker, there is currently no genetic determinate linked to nitric oxide levels and BiDil® response, and there is no easy method biochemically to measure nitric oxide levels. Therefore, reliance on race as a crude marker currently is necessary because no other non-racial population markers are available. While the action of BiDil® manufacturers in moving toward the racialization of the drug (procuring a significant extension in patent term and characterization of heart disease in blacks) may be motivated by economic considerations, as BiDil was shown to have statistically significant differences in efficacy between racial populations and because non-racial population markers are currently unavailable, BiDil® would be approved by the FDA under the recommended narrowly tailored regime of approving race-specific drugs.

### *Conclusions*

Race is a volatile social concept in the United States of which the scientific basis of race as a biologically significant categorization is hotly debated. The delineation of racial populations has changed throughout U.S. history and with the ever increasing population of multiracial individuals in the United States the line dividing racial populations is likely to blur even more. Genetically, race tends to be a very crude proxy for

---

primary end points to interpret the data. *Id.* at 15.

<sup>143</sup>See Anne L. Taylor et al., *Combination of Isosorbide Dinitrate and Hydralazine in Blacks with Heart Failure*, 351 NEW ENG. J. OF MED. 2049 (2004).

<sup>144</sup>See Rotman, *supra* note 12.

genetic variation. The limited usefulness of race as a genetic proxy is compounded by the fact that population differences for most complex disease genes will be the result, as least in part, of environmental factors. These environmental disease risk factors are often disproportionately prevalent in minority populations due to racial discrimination and socioeconomic disadvantage. Unfortunately, racial discrimination may only be further entrenched by the FDA approval of race-specific drugs as it may validate racist and eugenic ideological beliefs that there are innate genetic differences between racial populations. As this paper attempted to illustrate and likely inevitably oversimplified, the complexity of the term “race,” both socially and scientifically, is immense. Recognizing the complexity of race within the United States, the FDA should proceed cautiously in the further approval of race-specific drugs and review of race-specific new drug applications under a strict scrutiny regime. As drug manufacturers are making more race-specific drug claims, the issue of race-specific drugs is likely to arise more frequently within the FDA. The FDA needs to now develop and articulate a framework to guide the approval of race-specific medicines that minimizes the potential for discrimination and reinforcement of racist beliefs while still making safe and efficacious drugs available to all. In accordance with a strict scrutiny analysis and narrowly tailored use of race, the FDA should judiciously limit the FDA approval of race-specific drugs to situations in which the utilization of racial categories is based on statistically significant scientific data and necessity to ensure that access to safe and efficacious drugs is not a black and white issue.